

Kathleen D. Rigaut, Ph.D., J.D.
PTO Registration No. 43,047

Telephone: (215) 563-4100

Enclosures: Marked up copy of the claims showing where
amendments have been made

Copy of an abstract of the specification on a
separate sheet

Marked up draft of claims:

[26] 25. The method of claim 13 wherein a germline alteration is detected by obtaining a first CTSC gene fragment from (a) CTSC gene genomic DNA isolated from said sample, (b) CTSC RNA isolated from said sample or (c) CTSC cDNA made from mRNA isolated from said sample and a second CTSC gene fragment from a CTSC allele specific for one of said alterations, said second fragment corresponding to said first fragment, forming single-stranded DNA from said first CTSC gene fragment and from said second CTSC gene fragment, forming a heteroduplex consisting of single-stranded DNA from said first CTSC gene fragment and single-stranded DNA from said second CTSC gene fragment and analyzing for the presence of a mismatch in said heteroduplex, wherein no mismatch indicates the presence of said alteration.

[27] 26. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of a C for a T at nucleotide position 856 in Exon 6, thereby replacing a codon encoding glutamine for a stop codon.

[28] 27. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of an A for a G at nucleotide position 857 in Exon 6, thereby replacing a codon encoding glutamine for an arginine encoding codon.

[29] 28. A method as claimed in claim 13, wherein said germline alteration comprises a deletion of an A at nucleotide position 1047 in Exon 7, thereby causing a frameshift and a premature stop codon.

[30] 29. A method as claimed in claim 13, wherein said germline alteration comprises a deletion of a dinucleotide CT at nucleotide positions 1028 and 1029 in Exon 7, thereby

causing a premature stop codon.

[31] 30. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of a G for a A at nucleotide position 1286 in Exon 7, thereby replacing a tryptophan codon with a premature stop codon.

[32] 31. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of a C for a T at nucleotide position 1015 in Exon 7, thereby replacing a codon encoding arginine for a cysteine encoding codon.

[33] 32. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of an A for a G at nucleotide position 1019 in Exon 7, thereby replacing a codon encoding tyrosine for a cysteine encoding codon.

[34] 33. A method as claimed in claim 13, wherein said germline alteration comprises a substitution of an A for a G at nucleotide position 1040 in Exon 7, thereby replacing a codon encoding tyrosine for a cysteine encoding codon.

[35] 34. A method for detecting a germline alteration in a CTSC human encoding nucleic acid, said method comprising comparing a sequence of a CTSC DNA or CTSC RNA from a human sample with an isolated wild type CTSC sequence as provided in SEQ ID NO:1.

[36] 35. A method as claimed in claim 3[5]4, wherein stability of said altered CTSC mRNA is compared with stability of wild type CTSC mRNA.

[37] 36. A method as claimed in claim 3[5]4, further comprising expressing an altered CTSC protein from said altered CTSC encoding nucleic acid and comparing cathepsin C

enzymatic activity of said altered CTSC protein to enzymatic activity of wild-type cathepsin C.

[38] 37. A kit for detecting the presence of an altered CTSC encoding nucleic acid in a biological sample, comprising:

- i) oligonucleotides which specifically hybridize with CTSC encoding nucleic acids having the alterations set forth in Table 1;
- ii) reaction buffer; and
- iii) an instruction sheet.

[39] 38. A kit as claimed in claim [38]7, wherein said oligonucleotide contains a tag.

[40] 39. A kit for detecting the presence an altered CTSC encoding nucleic acid in a biological sample, comprising:

- i) antibodies immunologically specific for the altered CTSC proteins of the invention;
- ii) a solid support with immobilized CTSC antigens as a positive control; and
- iii) an instruction sheet.

[41] 40. A kit as claimed in claim [40]39, wherein said antibody contains a tag.